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National Institutes of Health (U.S.)
Division of Research Services.
Biomedical Engineering and
Instrumentation Branch.
Annual report.

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BIOMEDICAL ENGINEERING AND INSTRUMENTATION BRANCH

DIVISION OF RESEARCH SERVICES

NATIONAL INSTITUTES OF HEALTH

ANNUAL REPORT FY 1985

Dr. Murray Eden, Chief

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BEIB Research Projects (Z01 RS)

10001-17	Pharmacokinetics	R.L. Dedrick
10002-20	Implant Device Development	J.W. Boretos
10015-10	Development of Toposcopic Catheter for Clinical Vascular Use	D.R. Shook
10034-08	Three-Dimensional Histological Reconstruction	S.B. Leighton
10039-08	Biophysical Instrumentation and Methodology	M.S. Lewis
10043-08	Fiber Optics Probes	J.I. Peterson
10064-05	Indirect Blood Pressure Measurements in Laboratory Animals Using Oscillometry	E.C. Walker
10073-06	Secondary Emission Mass Spectrometer	L. Kelner
10096-05	Light Scattering Method for Evaluation of Platelets	R.F. Bonner
10097-05	Studies in Cardiovascular Dynamics	R.S. Chadwick
10098-05	Laser Instrumentation for Vitreous & Cardiovascular Microsurgery	R.F. Bonner
10099-05	Cochlear Mechanics and Hair Cell Transduction	R.S. Chadwick
10103-05	Triple Laser-Multi Parameter Flow Cytometry System for Study of Tumor Cell Kinetics	W. Schuette
10109-05	Adjunct Heat Treatment of Cancer	R.L. Levin
10110-05	A Dual 3-Dimensional Position Monitor For Speech Analysis: MOD. II	E.C. Walker
10112-05	Analysis of Microcirculatory Blood Flow by Laser Doppler Scattering	R.F. Bonner
10116-04	Modeling of Arterial Pulse Waves	R.S. Chadwick
10122-04	Micro-computer Controlled Fermentation System	T.R. Clem
10143-04	Interaction of Body Temperature and Sleep Rhythms	T.L. Talbot
10146-03	Prosthetic Urethral Sphincter	S.B. Leighton
10151-03	Nuclear Magnetic Resonance Imaging	D.I. Hoult
10153-03	A Position Sensor for Computer Modeling	H.E. Cascio
10156-03	Differential Scanning Calorimeter	C.P. Mudd
10157-03	Temperature Controlled Chamber for X-ray Diffraction Specimens	C.P. Mudd
10159-04	Pathophysiology of Cachexia in Sarcoma Patients	R. Corsey
10162-03	Wound Healing: Biology and Rheology	T.L. Talbot
10163-03	Magnetoencephalographic Localization of Foci of Neurologic Activity	P.D. Smith
10170-03	Biological Applications of a Computer Controlled Analytical Electron Microscope	R.D. Leapman
10184-02	Physical Chemistry of Biological Macromolecules	M.S. Lewis
10185-02	Interventional Catheter Development	J.W. Boretos
10187-02	Mixing During Intra-Arterial Infusion via Catheters	R.J. Lutz
10188-02	Drug Transport in Brain	P.F. Morrison
10191-02	Continuous Optical Monitoring for Bacterial Cultures	G.M. Maxwell

TABLE OF CONTENTS, (Cont'd)

10193-02	Development of Toposcopic Catheter for Clinical Gastroenterological Use	D.R. Shook
10194-02	Optimized Polymer Processing for Advanced Catheter Development	D.R. Shook
10201-01	Automated Cell Colony Scanner System	S.R. Goldstein
10202-01	Optical Techniques for Dental Instrumentation	G.M. Maxwell
10203-01	Clinical Assessment of Arterial Mechanical Properties	G.M. Maxwell
10204-01	Cell Handling Studies	S.B. Leighton
10205-01	Constant Shear Field Apparatus for ESR Studies	S.B. Leighton
10206-01	Concentration Uniformity by Diastolic Phasing of Pulsed Intra-Arterial Infusions	D.R. Shook
10207-01	Clinical Engineering Program for Hospital Patient Care Areas	R. Corsey
10208-01	Hemodynamic Principles in the Control of Coronary Blood Flow	T.L. Talbot
10209-01	Evaluation of Disposable Blood Pressure Transducers	E.C. Walker
10210-01	Electronic Patient Monitoring	H.E. Cascio
10211-01	IEEE-488 GPIB and Personal Computer Instrumentation Use Program Development	T.R. Clem
10212-01	Fluoroimmunoassay Apparatus	W.S. Friauf
10213-01	Vitreous Fluorophotometry Analysis	P.M. Bungay
10214-01	Photoradiation Therapy	P.D. Smith
10215-01	Measurement of Trace-Level Metals and Complexes in Biological Milieux	A.F. LeRoy
10216-01	Enzyme Purification - Calmodulin	A.F. LeRoy
10217-01	Compact, Time-Domain displays of Speech Signals	H.S. Eden
10218-01	Composition of Chromaffin Secretory Granules by Analytical Electron Microscopy	R.D. Leapman
10219-01	Quantitative Elemental Mapping of Rapidly-frozen Neural Tissue	R.D. Leapman
10220-01	Elemental Imaging of Alzheimer's Disease Related Brain Tissue	C.E. Fiori
10221-01	Elemental Imaging of Alveolar Macrophages	C.R. Swyt
10222-01	Elemental Distributions in Central Nervous System Tissues	C.R. Swyt
10223-01	Individual Human Peripheral Mononuclear Cell Magnesium Quantitation	G.R. Hook
10224-01	Modified Fourier Transform Techniques	M. Unser
10225-01	Processing of High Resolution Electron Micrographs	M. Unser

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10001-17 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pharmacokinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Dedrick	Chief, ChES	BEIB, DRS

Others:

F. Farris	North Dakota State University	BEIB, DRS
R. J. Lutz	Chemical Engineer	BEIB, DRS
F. King	Chemical Engineer	BEIB, DRS
P. F. Morrison	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*
CPB, NCI (J.M. Collins); LMCB-NCI (C.L. Litterst); DR-CC (J.L. Doppman); CP-CC (G. Hook); NTP-NIEHS (H.B. Matthews); SNB-NINCDS (E.H. Oldfield, C. Clark); University of Maryland (M.Egorin; M.F. Flessner).

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and man. They provide a plausible set of equations that can be used to extrapolate data from animals to man and thereby improve chemotherapy and risk assessment. Emphasis has been placed on regional drug administration, and this has led to the development of spatially distributed models of drug transport in tissue. These analyses have provided considerable insight into the penetration depths of drugs administered intraperitoneally or by infusion into the brain. The penetration of cis-dichlorodiammineplatinum (II) (DDP) into peritoneal and subperitoneal tissue is being examined experimentally with an electron probe and the results compared with a reaction-diffusion equation of the process. A lumped model of DDP pharmacokinetics has been developed to include both metabolism to a mobile species and covalent binding to macromolecules. Pharmacokinetic theory which was developed for intra-arterial drug administration combined with extracorporeal treatment of venous drainage had been validated in the clinic. Systemic exposure to DDP has been reduced by 49-74% by hemodialysis of jugular venous drainage during intracarotid artery infusion for the treatment of malignant glioma. Preliminary results have shown the feasibility of documenting appropriate vascular drainage with indocyanine green.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01-RS-10002-20-BEI

PERIOD COVERED
Oct.1, 1984 to Sept. 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Implant Device Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
John W. Boretos, Physical Scientist, BEIB, DRS

John Doppman, M.D.	Radiologist	CR, CC, NIH
Edward Oldfield, M.D.	Neurosurgeon	NINCDS, NIH
F.T. Hambrecht, M.D.	Health Science Adm.	NINCDS, NIH

COOPERATING UNITS *(if any)*
CR, CC, NIH; NS, NINCDS, NIH;
FNP, NINCDS, NIH;
BEIB, DRS, NIH.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, MD. 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.7	0.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to elucidate the interaction of biomaterials used for specific implants with the physiological environment and to explore specially prepared biomaterials and design features with respect to their suitability and performance in a variety of contexts. Polyurethanes are an important class of elastomers for use in catheters, heart assist pumps, electrode insulation and similar implant applications. Variations in the basic chemical structure of these polymers as well as physically induced stress can severely reduce their effectiveness for long-term use as a surgical device. Previous studies undertaken by this project have shown a relationship between the molecular chain structure in resisting hydrolytic forces. Recent evidence suggests that physical forces such as stress induced during fabrication can promote a form of stress corrosion. In vitro test data and SEM photomicrographs of surgical explants of various polyurethane classes show that premature failure is often the result of a combination of forces acting on the polymer at stress risers. A strong correlation exists between these in vitro and in vivo observations over short and long term periods of study.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10015-10 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Toposcopic Catheter for Clinical Vascular Use

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: D.R. Shook, Biomedical Engineer, BEIB, DRS
J.L. Doppman, Chief, DRD, CC
E.H. Oldfield, Senior Staff Neurosurgeon, SNB, NINCDS

COOPERATING UNITS *(if any)*
Diagnostic Radiology, CC (J.L. Doppman);
Surgical Neurology, NINCDS (E.H. Oldfield)

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.8	PROFESSIONAL: 0.3	OTHER: 0.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Toposcopy has been shown to be a reliable clinical means to catheterize long, small diameter, and highly tortuous blood vessels, inaccessible by previous techniques. A toposcopic element everts from the tip of a conventional catheter. This extremely flexible polyurethane element has been fabricated in 3, 4 and 5 French sizes mated with 5, 6 and 7 French catheters, respectively, and is capable of eversion lengths in excess of 40 cm.

The toposcopic catheter has been applied clinically for the local delivery of chemotherapy to brain tumors. Treatment is provided by positioning the conventional catheter in the internal carotid artery from a femoral entry; everting the toposcopic element through the carotid sinus, beyond the ophthalmic artery to avert retinal toxicity; and perfusing the tumor through the middle and/or anterior cerebral arteries. Not that a conventional catheter cannot safely negotiate the tortuosity of the carotid sinus.

The catheter has been extensively used clinically in its present prototype form, and production techniques for its fabrication are being transferred to private industry to provide for a ready source of catheters for future studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10034-08 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Three-Dimensional Histological Reconstruction

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
S.B. Leighton, Mechanical Engineer, BEIB, DRS
A.M. Kuzirian, Neuroanatomist, LB, NINCDS

COOPERATING UNITS *(if any)*
LB NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: .3	PROFESSIONAL: .3	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A semi-automatic system for acquiring three-dimensional structural information about histological material is being developed. The system should have significant speed and reliability advantages over present techniques using serial sections, although resolution may be limited. In brief, an embedded tissue block will be fixed relative to a scanning electron microscope imaging system, the surface of the block will be imaged and the image stored, and successive slices will be removed by a built-in microtome. Handling and registration of thin sections will thus be eliminated. Human and computer pattern recognition will transform the resulting set of images into a three-dimensional reconstruction. Oxygen plasma etching has been found to give sufficient topographic relief that the resolution of the images is now limited by the SEM and not by the preparation technique. The images of Hermissenda Crassicornis obtained by this technique correlate well with TEM images of the same tissue, indicating that the lack of artifact is adequate for the contemplated studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10039-08 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biophysical Instrumentation and Methodology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
Marc S. Lewis, Research Chemist, BEIB/DRS

Other: Thomas R. Clem, Electronics Engineer BEIB/DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Analytical Methods

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS: 0.1	PROFESSIONAL: 0.1	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project is designed to develop new instrumentation and methodology or improve existing instrumentation and methodology for characterization of biological macromolecules and for studying their interactions. Analytical ultracentrifugation, the techniques ancillary to it, and methods of data analysis using mathematical modeling appropriate for these techniques are the major areas of interest.

A microprocessor controlled system for the direct acquisition of data from the photomultiplier tube of the ultraviolet absorption scanner of the ultracentrifuge and for the control of that acquisition has been developed. The software requisite for making this system operational is presently in a developmental stage. When complete, this system will permit direct acquisition of data in digital form while the ultracentrifuge is operating and then permit preliminary data processing followed by transmission of the data to the DEC-10 computer for detailed analysis.

A study has been initiated on the possibility of development of new optical data acquisition systems for the conversion of current preparative ultracentrifuges into analytical ultracentrifuges with superior capabilities as analytical instruments at a fraction of the cost of the current instruments. Preliminary designs for such systems have been developed.

MLAB, operating on the DEC-10 computer, has been used for mathematical modeling studies for the analysis of various types of protein interactions. These studies have been applied to ultracentrifugal studies of binding and of protein self-assocation. Such studies are described in the project report entitled Physical Chemistry of Biological Macromolecules.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10043-08 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Fiber Optic Probes

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
John I. Peterson, Chemist, BEIB/DRS
Stephen E. Epstein, Chief, H IR CB

COOPERATING UNITS *(if any)*
H IR CB
H IR OD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.8	.8	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A suitable device is needed for the direct measurement of oxygen partial pressure (PO_2) in blood and tissue for both clinical and research applications. Methods currently available for measuring P02 lack convenience, reliability, speed, and relevance to many situations of interest. Efforts to develop electrical sensors have not been successful. It is desirable to have a very small P02 sensor which can be inserted into a blood vessel or tissue with little disturbance, and which will provide instantaneous and current P02 monitoring for either short or extended periods of time. A fiber optic sensor is ideal for this application, with the advantage, for physiological use, of very small size and flexibility, safety, and low cost. A P02 sensor has been developed, based upon the principle of fluorescence quenching by oxygen. The feasibility of the sensor and its satisfactory performance has been demonstrated in in vitro and in vivo tests, in work in preceding years. In the past year, the development of the sensor as a needle probe was accomplished, and problems of storage life and stability were resolved. This provides a basis for practical application of the fiber optic P02 probe as a research tool.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10064-05 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Indirect Blood Pressure Measurements in Laboratory Animals Using Oscillometry

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
E.C. Walker, Mechanical Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
SLAMS OD NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.25	PROFESSIONAL: 0.25	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Currently there are no reliable indirect methods of measuring blood pressure in dogs. Traditional techniques, used in humans, are unsatisfactory primarily because they require the placement of a transducer over the artery being monitored.

Because of the unreliability of traditional techniques we have been investigating a technique called oscillometry. Oscillometry is the method of measuring blood pressure by analyzing the pulse pattern of the cuff pressure oscillations.

In practice, a cuff is placed around a limb and inflated to a pressure above systolic and then deflated slowly. While the cuff is being deflated the amplitude of oscillation in cuff pressure, produced by the arterial pulse beneath the cuff, is monitored. Systolic and diastolic transitions in the oscillometric waveform are then used to indicate the indirect systolic and diastolic pressures respectively.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10073-06 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Secondary Emission Mass Spectrometer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

	L. Kelner,	Senior Staff Fellow,	BEIB, DRS
Others:	M. Eden	Chief	BEIB, DRS
	T. Patel	Chemist	BEIB, DRS

COOPERATING UNITS *(if any)*

LCS, NIMH (S.P. Markey), LC, NHBLI (H. Fales), DCRT, DRS (R. Tate)

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3	2.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

We have initiated a systematic study of the energetics of various organic ions in relation to the different experimental conditions ion SIMS and FAB analysis. Knowledge of the energy distribution (ED) of secondary organic ions helps us to understand the mechanism of organic sputtering and provides information for the optimization of liquid SIMS. Based on our previous data, we proposed that the primary mechanism responsible for the emission of secondary organic ions is linear cascade sputtering, as this process results in the production of ions with lower kinetic energy.

A major accomplishment in this FY was development-in collaboration with Teknivent. Inc.- of a data system based on an IBM PC-XT (256K), which was designed to control the quadrupole mass spectrometer of the SEMS system, and to scan the energy of secondary ions to produce energy distributions N(E)= f(E). The computer system was used to scan the main cylinder voltage (V_m) of the electrostatic energy analyzer (Bessel Box) as well as to control the tandem quadrupole mass spectrometer. The target bias (V_t) remained fixed during the energy scan, and the energy distribution was determined as a function of ion intensity versus (V_m-V_t). Complete spectra were stored for each step of the energy scan.

We have studied the energy distribution of secondary organic ions of arginine as wesl as effects of various liquid matrices on this parameter. Matrices employed included glycerol, triethanolamine, triethylglycol, and polyethyleneglycols, as well as protonating systems such as trifluoromethanesulfonic acid (TFMSA) and tartaric acid (TA).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10096-05 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Light Scattering Method for Evaluation of Platelets

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R. F. Bonner Physicist BEIB DRS

T.R. Clem	Elect. Engineer	BEIB DRS
S.B. Leighton	Mech. Engineer	BEIB DRS
J. Fratatoni	Dir. Blood Bank Products Branch	DBBP,CDB, FDA
B. Poindexter	Biologist	BBPB, DBBP, CDB, FDA
P. Mintz	Director	Blood Bank, U. Virginia

COOPERATING UNITS *(if any)*

Center for Drugs and Biologics, FDA
Blood Bank, U. Virginia

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Electronic Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Assessment of the functional status of platelets for transfusion is confounded by the inherent complexity of the cell, as well as the intricate requirements of sample preparation. A correlation between discoid shape and the functional integrity of the platelet has been established. We have developed a complex automatic machine based on previous experiments with a simple prototype which measures the fraction of the platelets that are discoid and the optical (volume) concentration of unaggregated platelets in standard blood bank platelet concentrate units within their bags. The microprocessor-based instrument automatically determines the volume concentration of unaggregated platelets and the fraction that are fully viable (discoid) during a 3-minute measurement sequence following simple insertion of the blood storage bag in the instrument. This process is noninvasive (sterile) and nondestructive. Thus it allows frequent measurements on the platelets prior to transfusion in order to optimize the quality and quantity of transfused platelets given patients. It also allows accurate investigations for optimizing storage and preparation methods. The instrument has been intensively studied with respect to invasive measurements of concentration and morphology of platelets and has proved to be highly accurate. In order to test the clinical significance of these measurements, a clinical evaluation of the instrumentation has begun at the Blood Bank of the University of Virginia.

Platelet reversible morphological changes in heating from 20 to 32°C have been discovered with the instrument and are being studied in order to better understand the relation between platelet in vitro and in vivo.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS-10097-05 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Studies in Cardiovascular Dynamics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S. Chadwick,	Biomedical Engineer,	BEIB, DRS
C. Oddou,	Professor,	University of Paris
P. Brun,	Senior Researcher,	INSERM U. 138
B. Levy	Senior Researcher,	INSERM U. 141
P. Peronneau,	Chief	INSERM U. 256

COOPERATING UNITS *(if any)*

INSERM U.138 U.141 U.256

University of Paris XII, Laboratory of Physical Mechanics

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.4	.4	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Our existing model for myocardial and ventricular mechanics will be refined to include an isotropic component of elasticity, passive and active viscoelasticity, non-cylindrical geometry, pathological fiber organization, and myocardial blood flow. The model will used in conjunction with ultrasonic kinematic data to determine performance parameters. The physiological relationships between phasic coronary arterial and venous pressure and blood flow, aortic input impedance and ventricular dimensions will be determined. A mathematical and physical model of myocardial blood flow will be developed incorporating vessel collapse. Experimental techniques will be developed to measure vascular distensibility in man. RF backscatter from the myocardium will be investigated both experimentally and mathematically with the idea of determining the stress field. Theoretical models of wave propagation in arteries and aortic input impedance will be checked with experimental data.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10098-05 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Laser Instrumentation for Vitreous & Cardiovascular Microsurgery

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
R.F. Bonner Physicist BEIB DRS

P.D. Smith Physicist BEIB, DRS

M. Leon	Sr. Investigator	CB, NHLBI
S. Epstein	Chief	CB, NHLBI
D. Underhill	Clinical Fellow	SB, NHLBI
R. Clark	Chief	SB, NHLBI
R. Nossal	Sr. Res. Physicist	PSL, DCRT

COOPERATING UNITS *(if any)*
Clinical Branch, NEI
Cardiology Branch & Surgery Branch, NHLBI.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 1.3	PROFESSIONAL: 1.3	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study entails the development and methodology of use of pulsed carbon dioxide laser systems, pulsed Nd:YAG laser coupled to a slit lamp, Q-switched Excimer lasers, and high-power CW Argon laser with fiber-optic delivery systems. For the CO_2 and Nd:YAG laser systems systematic studies of animal vitrectomies were performed in order to characterize laser pulse characteristics necessary to transect vitreal membranes. Additional studies of retinal damage as a function of pulse characteristics and distance of cutting site from the retina clarified the potential for use of these laser systems close to the retina.

For all laser systems systematic studies of tissue damage on human coronary arteries was performed so as to determine their feasibility (and optimal system design) for laser angioplasty. The Argon laser/ fiber optic system was able to ablate artery wall and non-calcified plaque when probe was kept in contact with the bottom of the crater as it was formed. Argon laser systems could not ablate calcified lesions. High power nanosecond (or shorter) duration Nd:YAG laser pulses could easily remove noncalcified plaque but removed calcified plaque only very slowly. Additionally large fissures in the artery wall occured, most likely the result of shock waves created by the transient absorption of the laser energy. Submillisecond CO_2 laser pulses ablated tissue with minimal thermal damage to surrounding tissue. Excimer laser pulses etched very clean craters in calcified as well as non-calcified plaque.

Evaluation of prototype fiber-optic laser angioscopes in animals were carried out to evaluate this technology as an adjunct to surgery and as an aid in directing laser angioplasty. Human fiber-optic angioscopy during bypass surgery has been initiated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10099-05 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cochlear Mechanics and Hair Cell Transduction

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S Chadwick,	Biomedical Engineer	BEIB,	DRS
J. Rinzel,	Chief	MRB,	NIADDK
S. Shamma,	Assistant Prof. Univ. of MD, Dept. of Electrical Engineering		
J. Wilbur,	Staff Fellow,	MRB,	NIADDK
K. Morrish	Staff Fellow	MRB,	NIADDK

COOPERATING UNITS *(if any)*
NIADDK, Mathematical Research Branch
Univ. of Maryland, Dept. of Electrical Engineering

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A mathematical model of cochlear processing is developed to account for the nonlinear dependence of frequency selectivity on intensity in inner hair cell and auditory nerve fiber responses. The model describes the transformation from acoustic stimulus to intracellular hair cell potentials in the cochlea. It incorporates a linear formulation of basilar membrane mechanics and subtectorial fluid-cilia displacement coupling, and a simplified description of the inner hair cell nonlinear transduction process. The analysis at this stage is restricted to relatively low frequency single tones. The computed responses to single tone inputs exhibit the experimentally observed nonlinear effects of increasing intensity such as the increase in the bandwidth of frequency selectivity and the downward shift of the best frequency. In the model the first effect is primarily due to the saturating effect of the hair cell nonlinearity. The second results from the combined effects of both the nonlinearity and the inner hair cell lowpass transfer function. In contrast to these shifts along the frequency axis, the model does not exhibit intensity dependent shifts of the spatial location along the cochlea of the peak response for a given single tone. The observed shifts therefore do not contradict an intensity invariant tonotopic code.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10103-05 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Triple Laser-Multi Parameter Flow Cytometry System for Study of Tumor Cell Kinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W. Schuette, Chief, ACES, BEIB, DRS
S. Shackney, Allegheny General Hospital, Pittsburg, PA 15212
J. Dvorak LPD-NIAID
F. Plowman, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*

DRS-NCI
LPD-NIAID

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 3	PROFESSIONAL: 2	OTHER: 1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A triple laser flow cytometer has been developed so that various immuno-fluorescent labeling techniques may be employed for the investigation of cell kinetics. Three laser beams at different wave lengths are made to intersect a tumor cell flow stream passing through a quartz cuvette so that multi-parameter signals may be obtained. These signals are processed by specialized electronics and then analyzed by means of a PDP 11 computer. Simplified optics have increased light detection efficiency by an order of magnitude. The system is currently being used for the investigation of a unicellular protozoon known as trypanosoma cruzi, the causative agent of Chagas disease. Electronic cell volume capability has been added to the system to assist in the bivariate analysis of trypanosoma cruzi fluorescence data.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10109-05 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Adjunct Heat Treatment of Cancer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Levin, Biomedical Engineer, BEIB, DRS
M. Hagmann, Senior Staff Fellow, BEIB, DRS
J-L Guerquin-Kern, Fogarty Fellow, BEIB, DRS
C. Charny, Guest Worker, BEIB, DRS
A. Shitzer, Visiting Scientist, BEIB, DRS
A. Zabel, Physician, ROB, NCI
E.J. Glatstein, Chief, ROB, NCI

COOPERATING UNITS *(if any)*
Radiation Oncology Branch, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.8	3.8	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to facilitate the development of adjunct hyperthermia modalities for cancer treatment by theoretically and experimentally studying the spatial and temporal variation in the temperature field of tissues subjected to microwave and radio-frequency electromagnetic radiation. Currently, we are (1) experimentally measuring the patterns of energy deposition within various types of extremity phantoms produced by a Mini Annular Phased Array (MAPA) applicator; (2) theoretically describing the electromagnetic fields of a MAPA in terms of its design paramters; (3) theoretically describing the transient thermal profiles within limbs produced by a MAPA; and (4) theoretically describing the systemic temperature and cardiac changes associated with heating various regions of the body. We are also performing electromagnetic and thermal modeling of the unwanted non-local energy deposition occuring outside the bounds of typical hyperthermia applicators.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10110-05 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Dual 3-Dimensional Position Monitor For Speech Analysis: MOD. II

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E.C. Walker, Mechanical Engineer, ACES BEIB

Other Investigators
H.W. Tipton, Mechanical Engineering Tech. ACES BEIB
T.L. Talbot, Mechanical Engineer ACES BEIB
C.L. Ludlow, LCD NINCDS
M. Doran-Quine, Guest Researcher NINCDS

COOPERATING UNITS *(if any)*
LCD-NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.5	.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Several speech monitoring instruments have been designed to study the etiology of normal and abnormal articular movements in humans. The first system, which is in current use, provided a unique method of monitoring 3-D lip and jaw movements. The second system, MOD II, is an improved version of the first. The device consists of two mirror image transducers mounted on a common head frame. Each transducer, which can be individually adjusted, is capable of measuring the movement of a point in three orthogonal planes. The transducers have been structurally and operationally redesigned to provide increased linearity, resolution, and reduced weight. Additionally, the head frame has been totally redesigned to provide improved wearing comfort and reduced weight. The improved system will facilitate studying a broader patient population such as children and the elderly.

Design and fabrication of MOD II has been completed. Results of bench tests indicate that the system performs well, within its specified range. Future efforts will be directed toward patient testing.

Following system enhancement, patient testing will be scheduled for the upcoming fiscal year.

Due to the patient population (which includes dysarthric patients) that this device is designed for, future enhancements will include improved resolution along the lateral-medial axis and reduction of inertial response.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10112-05 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Analysis of Microcirculatory Blood Flow by Laser Doppler Scattering

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
R.F. Bonner, Physicist, BEIB, DRS
T.R. Clem, Elect. Engineer, BEIB, DRS
M. Kaliner, Section Chief LCI NIAID
H. Druce, Clinical Assoc. LCI NIAID
G. Rogers, Clinical Assoc. LCI NIADDK
M. Roy, Visiting Scientist NEI
D. Goldstein, Sr. Invest. HB NHLBI; H. Kaiser, Chief HB NHLBI
E. Oldfield, Neurosurgeon SN NINCDS; R. Blacklock, Clinical Assoc. SN NINCDS

COOPERATING UNITS *(if any)*
Hypertension Br., NHLBI; Lab of Clinical Investigation, NIAID; Lab of Chemical Biology, NIADDK; Surgical Neurology, NINCDS; Clinical Branch, NEI; MED Pacific, Inc. Seattle, Washington; TSI, St. Paul Minn.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 1.6	PROFESSIONAL: 1.6	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is the development of a clinical, non-invasive monitor of tissue blood flow by analysis of the spectrum of Doppler-scattered laser light. The NIH Laser Doppler Blood Flow Monitor has been demonstrated to be highly portable and clinically convenient with sterilizable, rugged flexible 4m fiber optic probes and portable photodiode detection system. The linearity of the flow analysis processor has been demonstrated in a variety of tissues and clearly resolves physiologic flow changes including pulsatile flow in the microcirculation. Muscle blood flow in over 50 patients with neuromuscular disease has been studied and data suggest that post occlusive reactive hyperemia responses may be primary or secondary indicators of disease state. Measurements of local muscle blood flow dynamics in patients with neuromuscular diseases indicate abnormalities distinct to different disease types. Nasal blood flow has been shown to be a quantitative measure of the physiologic response of the nose to drug challenges. Brain and spinal cord blood flow measurements during microsurgery has been shown to be feasible in two patients and provides the surgeon with potential for useful evaluation of his surgical procedures as well as for furthering understanding of microcirculatory dynamics in neural tissue. Studies show a characteristic local oscillatory flow pattern in a capillary microcirculation of the skin in sickle cell patients which appears to correlate with severity of disease and its response to drug therapy. Similar oscillations presumably due to myogenic arteriolar smooth muscle vasomotion are characteristic of several hypertensive patients, particularly those on drugs inducing peripheral vasocontriction. Preliminary studies on patients with Type I diabetes have shown abnormalities potentially related to the etiology of the microvascular component of long-term type I diabetes. In summary numerous ongoing clinical studies seek to characterize microvascular functional abnormalities and their role in a number of diseases with microvascular components.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10116-04 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Modeling of Arterial Pulse Waves

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S. Chadwick,	Biomedical Engineer,	BEIB,DRS
D. McGuire,	Mathematician,	BEIB
J. Tenney,	Biomedical Engineer	BEIB
D. Goldstein ,	Senior Investigator	EHL, NHLBI
H. Kaiser,	Chief EHL,	NHLBI

COOPERATING UNITS *(if any)*
NHLBI, Endocrine-Hypertension Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.6	.3	.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A pulse wave theory and a model of the human brachial arterial system is developed that predicts the changes in the arterial pressure waveforms as it traverses the vasculature - increased pulse, sharper main wave, disappearance of the aortic incisura, and appearance of a diastolic dicrotic wave. It also predicts the observed modulation of the waveform during phenylephrine - induced vasoconstriction and nitroglycerin - induced vasodilation. The model considers the brachial arterial system as a tapered distensible tube ending in a loop, with side branch networks represented by distributed Windkessels, and it uses verifiable values for realistic parameters. We found that the vertical modulation of the dicrotic wave in people decreased with advancing age and with high blood pressure, the model explaining these finding in terms of increasing vascular rigidity and decreasing small vessel vasodilator responsiveness. We noted a significant negative correlation between the arterial level of plasma norepinephrine and the amount of modulation of the dicrotic wave after nitroglycerin among subjects 40 years old or younger, suggesting a sympathetic neurogenic contribution to the vascular abnormalities observed in relatively young patients with essential hypertension.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10122-04 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Micro-computer Controlled Fermentation System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.R. Clem, Sr., Electronic Engineer, EEES, BEIB, DRS

Other Investigators:

Y. Shiloach	Chief, Pilot Plant	LCDB NIADDK
A. LeRoy	Chemical Engineer	BEIB, DRS

COOPERATING UNITS *(if any)*
LCDB - NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.5	0.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A process control system using a Personal Computer as the central control element is continuing to be developed for the NIH Fermentation Pilot Plant. The various monitoring transducers and controlled elements (pumps, valves, etc.) are connected to the computer via the IEEE-488 General Purpose Interface (GPIB) and special purpose interface cards. For maximum versatility most components used are commercially available items (instruments, meters, etc.). The PC-based design allows changes in the parameters measured or controlled, or scaling to different size vessels to be accomplished relatively quickly and easily. Utilizing the computational capabilities of the computer/controller allows initial selection of the operating parameters and dynamic alteration of these parameters as the process continues, thus allowing optimization of yields or detailed study of the process parameters.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10143-04 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Interaction of Body Temperature and Sleep Rhythms

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.L. Talbot, ACES, BEIB, DRS
Wallace Mendelson, Psychobiology, NIMH

COOPERATING UNITS *(if any)*
Psychobiology Lab-NIMH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Clinical evidence suggests a correlation between core body temperature and the frequency of sleep episodes. An artificial thermoregulatory system is completed which will permit core body temperature manipulation and hence, the evaluation of the efficacy of thermal regulation in the treatment of sleep disorders. Clinical trials are now performed on a regular basis. Simultaneous sleep recordings are obtained during both a non-manipulated and manipulated 24 hour period.

Clinical studies are now underway and the data obtained so far suggests no interaction between sleep rhythms and body temperature. More studies are being performed to substantiate conclusively these findings.

Reevaluation of clinical evidence has prompted an extensive effort to accumulate a larger, more complete data base of control subjects. Standard sleep recordings and temperature profiles of normal subjects are being taken before further intervention protocols are implemented.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10146-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Prosthetic Urethral Sphincter

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S. B. Leighton, Mechanical Engineer, BEIB, DRS,
Steven Scoog, M.D. WRAMC
T. Rade Baugh, BRCM, NIA

COOPERATING UNITS *(if any)*
BRCM, NIA
DCT, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: .05	PROFESSIONAL: .05	OTHER: 0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A number of techniques are used for treating urinary incontinence, including a number of artificial prosthetic sphincters. The present work concerns an entirely intraurethral artificial sphincter that can be implanted without surgery. Concepts are being explored which would allow the device to be used in situations in which surgery is contraindicated, and would also presumably lower the cost. The valve would be appropriately matched to urethral dimensions, pressures, and flowrates. The valve would be potentially useful in cases of nonopening normal valves as well as in cases of non-closing valves.

PHS 6040 (Rev. 1/84)

GPO 914-918

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10151-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Nuclear Magnetic Resonance Imaging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Dr. David I. Hoult, Physical Scientist, BEIB, DRS

Other personnel:
Dr. Ching-Nien Chen, Expert
Dr. Victor J. Sank, Expert
Dr. L. Kyle Hedges, Staff fellow

COOPERATING UNITS *(if any)*
Department of Radiology, Clinical Center

LAB/BRANCH
NMR Imaging Laboratory, Biomedical Engineering and Instrumentation

SECTION
Office of the Chief

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 3.2	PROFESSIONAL: 3.0	OTHER: 0.2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Using our previously developed nuclear magnetic resonance imaging equipment, the dependence of the signal-to-noise ratio and radio frequency power deposition in patients, as a function of static field strength, has been investigated, in order to elucidate further the factors influencing the choice of a field strength for clinical imaging. It has been found that power deposition in the torso is reduced by a factor of between 1.5 and 2.5 (depending on patient build) if the irradiating field is applied laterally, as opposed to anterior-posterior, and the signal-to-noise ratio dependence has been shown to be in good agreement with a previously developed theory. Quadrature coil development has progressed well for imaging and for spectroscopy. Improvements have been made, with the aid of pieces of steel, to the homogeneity of the clinical imaging instrument.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10153-03 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Position Sensor for Computer Modeling

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H. E. Cascio, Electronic Engineer, BEIB, DRS
P. Smith, Physicist, BEIB, DRS
S. Leighton, Mechanical Engineer, BEIB, DRS
R. Feldmann, CCB DCRT

COOPERATING UNITS *(if any)*
CCB, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.50	PROFESSIONAL: 0.20	OTHER: 0.30

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For the study of macromolecular structure and of molecular interactions, the use of a computer generated display of the molecule is a powerful interpretive tool. In particular, the ability to be able to manipulate in space, i.e. to rotate and translate the molecule(s) to any desired orientation enhances the usefulness of the device. A further degree of sophistication is to provide a feedback mechanism giving an indication of the repulsive or attractive forces (Van der Waals interactions) present as two molecules are fitted together or as a single molecule is twisted to a new conformation. A joy stick apparatus has been designed to provide these features. Two molecules or part of the same molecule can then be rotated and translated in any direction. With each new position, the computer program re-evaluates the appropriate forces to provide the investigator with a feel of the total forces involved.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10156-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Differential Scanning Calorimeter

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS
T. Talbot, Mechanical Engineer, ACES, BEIB, DRS
P.D. Ross, Physical Chemist, A LMB, NIADDK

COOPERATING UNITS *(if any)*
A LMB, NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda. MD 20205

TOTAL MAN-YEARS: 0.2	PROFESSIONAL: 0.2	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The application of sensor design and modelling techniques from earlier work in differential heat conduction calorimeters to DSC (differential scanning calorimeters) has produced a prototype DSC with a 10 fold effective increase in sensitivity. The effective increase in sensitivity is due to two factors: 1) new thermopile design with increased electrical sensitivity, and 2) improved cell mounting techniques, which increased the common mode rejection of the system. A four channel laboratory instrument based on this prototype design is now being fabricated and will be evaluated in late 1985.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10157-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Temperature Controlled Chamber for X-ray Diffraction Specimens

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS
H.W. Tipton, Mechanical Engineering Tech., ACES, BEIB, DRS
A.V. Parsigian, Researcher, CR, PSL
B.K. Lee, Researcher, CR, PSL
D. Rau, A, LCP

COOPERATING UNITS *(if any)*
DCRT, CR-PSL

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.2	PROFESSIONAL: 0.2	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A prototype chamber was constructed of lexan and aluminum with a beryllium window to allow the entry of the x-ray beam. The cell containing the specimen is loaded into a holder next to the window. The bottom of the holder is held in contact with one side of a Peltier solid state heat pump. The opposite side of the heat pump is clamped to the aluminum bottom of the chamber which serves as the heat sink. In this early version, a thermistor was used to control the heat pump to keep the specimen at the set temperature. The film plate is mounted inside the chamber on an adjustable slide. Based on the performance of this prototype, two chambers with different focal lengths were requested. The new units were designed with an improved temperature controller. The new unit incorporates a linear feedback sensor with a bipolar supply to allow automatic switching from cooling to heating. The set temperature is fixed by a 3 digit thumbwheel switch and the sample temperature is read out on a $3^1/2$ digit display. This new system will hold the sample temperature between -3°C and 85°C with a stability of 0.02° C.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10159-04 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pathophysiology of Cachexia in Sarcoma Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
R. Corsey, Electronic Engineer BEIB, DRS

J.A. Norton Section Chief SURG, NCI
R. Inculet, Research Associate, NCI

COOPERATING UNITS *(if any)*
Anesthesia Service, Clinical Center, NIH
Nutrition Department, Clinical Center, NIH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.5	0.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

9 volunteers and 5 patients have been studied. The goal is to study 30 volunteers and 20 patients after which the following questions will be asked:

1. Are patients with preoperative sarcoma different from controls with respect to resting energy expenditure, glucose oxidation whole body protein turnover and k90 levels different in preoperative sarcoma patients from controls?
2. Do differences detected correlate with tumor size or tumor protein fractional synthesis rate?
3. Do differences detected disappear with resection of the tumor?

Patients and volunteers are seen by a dietitian who performs a nutritional assessment and estimation of resting energy expenditure. Calorimetry, mass spectrometry and k40 determinations using a whole body counter are performed preoperatively. Protein metabolism and muscle and tumor fractional synthesis rates are measured using 13C-leucine and 15N-glycine.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10162-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Wound Healing: Biology and Rheology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Thomas L. Talbot, MS, ACES, BEIB
Walter T. Lawrence M.D., C. Surgery, NCI
Lawrence E. Thibault, ScD. Bioengineering Dept, Univ. of Pa

COOPERATING UNITS *(if any)*
NCI, University of Pa, Philadelphia, Pa

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	1	0.2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Preliminary studies have been completed with swine models. These studies involved stamping an indelible grid (10cmx10cm) on the skin of the swine, and the excision of a 1 cm by 10 cm strip of the skin out of the grid area, and finally approximating the incision edges with silk sutures. Photographs of the grid were taken before excision, after excision, and after suturing. These photographs will be analyzed to determine the impressed strain on the wound closure and eventually relate this information to wound breaking strength (WBS).

Studies based on a rat model that relate biologic and pharmacologic interventions to WBS have been completed. Certain groups were treated pharmacologically during the wound healing process. Significant decrease in WBS was observed in these groups as compared to control groups. Further studies will include the comparison of tumor bearing group to control groups.

Rats treated with 8 mg/kg Adriamycin prior to or on the day of wounding demonstrated decreased wound breaking strength in incisional wounds at all intervals after wounding. Decreased amounts of collagen and DNA, lower mitotic rates, and decreased cellularity were noted in wound chambers from rats treated in this manner. In both the incisional wound and wound chamber models, rats treated with Adriamycin seven days after wounding showed a less dramatic healing impairment. No differences in collagen type were noted between chambers from the Adriamycin treated and untreated rats. The data suggest that deficient quantities of platelet, macrophage, and lymphocyte factors; a decreased rate of collagen synthesis, and impaired collagen remodelling all contribute to the Adriamycin induced healing impairment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10163-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Magnetoencephalographic Localization of Foci of Neurologic Activity

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D. Smith	Physicist	BEIB, DRS
R.F. Bonner	Physicist	BEIB, DRS
W.S. Friauf	Section Chief	BEIB, DRS
S. Sato	Sr. Investigator	EB NINCDS
R. Porter	Chief	EB NINCDS
M. Nisenoff	Chief	NRL

COOPERATING UNITS *(if any)*
Epilepsy Branch, NINCDS; Naval Research Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	0.5	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continued collaboration with the Naval Research Laboratories has enabled a SQUID magnetometer to be used to study inter-ictal spike discharges in epileptic patients. Correlation of the MEG activity and the corresponding EEG signal for these discharges permits signal averaging of spikes associated with the same neurological event. These measurements allow a magnetic field map at the surface of the scalp to be obtained from which a prediction of the source of the epileptic focus can be made. Computer and electronic processing techniques have been developed to analyze these MEG and EEG signals with the aim of producing an efficient method of localizing the sources of the epileptic discharges in a selective manner. Several patients have been scanned using these techniques. To enhance the collection of MEG data associated with a single spike discharge, a seven channel array detector has been specified and will be installed shortly.

Magnetic field maps generated on patients going to surgery predicted epileptic source localization consistent with intraoperative electrical recordings. Refinements of the mapping procedures including MEG normalization by EEG spike amplitude and modeling of contributions of non-sphericity of the scalp over the temporal lobe appear to be substantial improvements in the state-of-the-art.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10170-03 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biological Applications of a Computer Controlled Analytical Electron Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Visiting Scientist	BEIB, DRS
Others:		
C.E. Fiori	Physical Scientist	BEIB, DRS
C.R. Swyt	Physical Scientist	BEIB, DRS
K.E. Gorlen	Electronic Engineer	CSL, DCRT
C.C. Gibson	Electronic Engineer	BEIB, DCRT

COOPERATING UNITS *(if any)*
DCRT, NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.5	2.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Further advances have been made in the capabilities of the computer controlled analytical electron microscope, developed jointly by BEIB and DCRT, and the instrumentation has been applied to several biological problems in the past year. Two of these studies involved extensive electron energy loss spectroscopy. The newly installed Gatan 607 magnetic sector energy loss spectrometer has been shown to be fully corrected for second order aberations. This has permitted a significant improvement in collection efficiency and energy resolution while allowing concurrent acquisition of energy dispersive x-ray (EDXS) and electron energy loss spectra (EELS) as well as simultaneous elastic dark field imaging in the scanning transmission mode. A basic study has been carried out to characterize the peak shapes of the x-ray detectors, and this has led to modifications to the Tracor Northern detector in order to improve performance.

EELS and EDXS elemental maps and spectra have been obtained from pancreas beta cells prepared by rapid freezing, freeze-drying (or freeze-substitution) followed by embedding in order to investigate the composition of the secretory granules. Spectra have been quantitated to determine ratios of elements in the insulin-containing granule cores. A feasibility study has been made for obtaining low dose EELS maps using averaging procedures in periodic crystalline arrays of membranes. Data have been obtained from thin samples of reconstituted porin membrane containing lipid and protein sub-units and transmembrane channels. Both the experimental data and theoretical signal/noise estimations suggest that low dose elemental mapping should be possible.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10184-02 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Physical Chemistry of Biological Macromolecules

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Marc S. Lewis Research Chemist, BEIB/DRS

S.I. Chung	Research Chemist	LB NIDR
G.W. Laurie	Visiting Fellow	LBDA NIDR
G.R. Martin	Laboratory Chief	LBDA NIDR
R.J. Youle	Research Chemist	SNB NINCDS

COOPERATING UNITS *(if any)*
LB/NIDR, LBDA/NIDR, SNB/NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis, O. Ch.

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS: 0.9	PROFESSIONAL: 0.9	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to study the physical properties of a wide variety of biological macromolecules with the goal of correlating these properties to the structure and function of the macromolecules. The emphasis is on the thermodynamics of the interactions of these macromolecules and on their molecular size and shape. Analytical ultracentrifugation and mathematical modeling are the principal research techniques used.

Studies on the association of fibrinogen with other proteins involved in blood clotting and fibrinolysis have been continued. Studies currently in progress in this area deal with the association of fibrinogen with plasma and platelet Factor XIII and with the associaiton of plasminogen with the D and E fragments of fibrinogen.

Studies on the association of the A and B chains of reduced ricin indicate that the formation of the AB complex is reversible and that the temperature dependence of this reaction indicates that it appears to be entropically driven, suggesting that there is a strong hydrophobic interaction between A and B chains even in the absence of the disulfide bond. Cell toxicity studies indicate that reduced ricin is more toxic than native ricin at high concentrations, indicating that the disulfide bond between the chains is not necessary for biological activity.

The small and large forms of heparin sulfate proteoglycan isolated fdrom EHS tumor basement membrane have been studied by electron microscopy and by analytical ultracentrifugation. These studies indicate that these proteoglycans show similarities in the number and size of the heparin sulfate side chains but differ in the length of the protein core.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10185-02 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Interventional Catheter Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

John W. Boretos, Physical Scientist, BEIB, DRS

Others:

John Doppman, M.D.	Radiologist	CR, CC, NIH
Edward Oldfield, M.D.	Neurosurgeon	NINCDS, NIH
Robert L. Dedrick, Ph.D.	Chem. Engr.	BEIB, DRS, NIH

COOPERATING UNITS *(if any)*
CR, CC, NIH; NS, NINCDS, NIH,
BEIB, DRS, NIH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.4	0.7	0.7

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of the project is to develop a catheter system for interventional radiology which is capable of traversing small and branching blood vessels (i.e. 1.5 to 4.0 mm) to reach the proximity of tumors and to administer chemotherapeutic drugs to these tumors in a controlled manner. A major obstacle to effective treatment is thought to be maldistribution of the drug at the site due to inadequate mixing with the blood. A multi-lumen catheter, which is propelled and directed through these small blood vessels via jets of fluid emanating from its distal end, continues to show promise for negotiating heretofore difficult to reach areas. Fluid turbulence generated by drug emanating at retrograde angles from the tip of the catheter adds significantly to the mixing of the drug within the blood stream. Animal tests have substantiated the feasibility of the catheter system for clinical use. A transparent model of the vascular network simulating blood flow of a pulsatile nature was designed to evaluate the efficiency of the jet flow at various delivering rates. A high torque roller pump using custom designed polyurethane tubing is capable of producing satisfactory infusion rates over an 8 hour period.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10187-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Mixing During Intra-Arterial Infusion via Catheters

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.J. Lutz	DRS, BEIB	J. Boretos	DRS	BEIB
R.L. Dedrick	DRS, BEIB	C. Thompson	DRS	BEIB
B. Blacklock	NINCDS, IR, SN	R. Pflueger	DRS	BEIB
E. Oldfield,	NINCDS, IR, SN			
J. Doppman	CC, DR			
D. Miller	CC, DR			

COOPERATING UNITS *(if any)*
NINCDS
CC

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.0	.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Intra-arterial chemotherapy offers an alternative to systemic (iv) chemotherapy for localized neoplasms. Infusion of chemotherapeutic agents directly into the arterial supply of the neoplasm allows, under proper circumstances, higher local tissue concentrations without a corresponding increase in systemic toxicity. Results using this treatment method in patients have varied. In some instances, cases of severe ophthalmic toxicity and of leukoencephalopathies have been reported. These findings suggested the possibility that streaming of the infused drug solution resulted in inadequate mixing and therefore non-uniform drug concentrations in the infused tissue region. Fluid-mechanical studies with an in vitro model of a human carotid artery system have demonstrated that streaming can occur at low infusion rates, and that mixing can be enhanced by increasing the infusion velocities and also by improving the design of the catheter tip, such as injecting transversely or retrograde to the artery flow. In vivo studies involving both slow and fast infusions of radiolabeled iodoantipyrine into the carotid artery of monkeys and subsequent autoradiographic analysis of brain slices have corroborated the findings of the in vitro model studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10188-02 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Drug Transport in Brain

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.F. Morrison	Physical Scientist	BEIB, DRS
R.L. Dedrick	Chief, ChE Section	BEIB, DRS
E.H. Oldfield	Neurosurgeon	SN, NINCDS

COOPERATING UNITS *(if any)*
Surgical Neurology Branch, NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The transport and reaction of cisplatin in the brain of the rat has been investigated with the intent of refining estimates of associated parameters. These parameters are needed to prospectively model various tumor treatment modalities for expected efficacy.

A steady-state reaction-diffusion model was capable of representing the total platinum concentration profiles in the cerebellum following a continuous 7-day infusion of drug. The infusate cannula was treated as a point source and flow of drug into CSF was shown to be negligible.

Reaction of cisplatin with the sulfur-containing moieties of cells was examined in detail. Saturation of binding sites, primarily composed of cysteine, methionine, and some histidine residues, was found to occur within 1 mm of the cannula tip. Saturation was modeled approximately as the reaction of free cisplatin with the time-averaged unbound protein concentration. At distances far from the cannula, e.g. 4 mm, protein degradation products containing platinum begin to contribute to the total platinum profile but they were shown to account for only about 3% and no more than 20% of the total present.

The best linear reaction rate of cisplatin with protein was found to be .005 .002 min(-1). Inclusion of convection effects near the cannula tip decreases this value, but by no more than 30%, while saturation effects tend to increase it by about 40%. The capillary permeability was found to equal 9.0x10(-7) cm/sec and be nearly unaffected by saturation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10191-02 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Continuous Optical Monitoring for Bacterial Cultures

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
G.M. Maxwell, Staff Fellow, BEIB, DRS
S.B. Leighton, Senior Engineer, BEIB, DRS
Ernst Freese, Chief, LMB, NINCDS

COOPERATING UNITS *(if any)*
LMB, NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.25	.25	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The incubation of bacterial cultures is a standard laboratory technique in numerous biological studies. Monitoring the growth of these cultures in a shaker bath or fermentor currently requires frequent manual sampling. The work on this project has been aimed at developing a system capable of continuously monitoring growth in situ using optical measurement techniques.

To date the work has demonstrated the feasibility of making these measurements in shaker flasks employing an immersed detection system and yielded a prototype system for this application. Additional efforts have been directed at designing a system which will operate in a commercial type fermenter. The principal problem of eliminating gas bubbles in the optical path of the immersed probe has been solved.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10193-02 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Toposcopic Catheter for Clinical Gastroenterological Use

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

D.R. Shook, Biomedical Engineer. BEIB,DRS

COOPERATING UNITS *(if any)*
Naval Hospital Bethesda, Naval Medical Command, National Capital Region, USN (E.L. Cattau, T.J. Spurling); Esophageal, Gastric and Colonic Diseases, Digestive Diseases and Nutrition Division, NIADDKD (K.J. Vener).

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The unique characteristics of the toposcopic catheter have suggested its application in the gastrointestinal system. The operation of the catheter promises to facilitate the catheterization of the pancreatobiliary ducts through the Papilla of Vater. An initial series of patients has undergone routine endoscopic retrograde cholangiopancreatography (ERCP) using the topocatheter for contrast infusion. An extensively modified topocatheter is passed through an appropriately positioned endoscope. The catheter tip is placed within the ampulla, and the toposcopic element is everted. In basic ERCP, contract medium is then injected for appropriate diagnostic procedures. In addition, the topocatheter's ability to atraumatically negotiate small, tortuous ducts is being applied to catheterization of remote pancreatic and cystic ducts for sampling of pure secretions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10194-02 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Optimized Polymer Processing for Advanced Catheter Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

D.R. Shook, Biomedical Engineer, BEIB, DRS
B. Bourin, Guest Researcher, BEIB, DRS

COOPERATING UNITS *(if any)*

Diagnostic Radiology, CC (J.L. Doppman); Esophogeal, Gastric and Colonic Diseases, Digestive Diseases and Nutrition Division, NIADDKD (K.S. Vener)

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering Section,

INSTITUTE AND LOCATION

National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.6	PROFESSIONAL: 0.5	OTHER: 0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Advanced techniques of plasticating extrusion can produce materials of optimized anisotropic properties and very fine dimensional characteristics. Availability of such materials then supports development of unique polymeric medical devices, such as the toposcopic catheter. Unique polymer resins are first characterized specifically for extrusion characteristics, and predictive models of rheological behavior are constructed. Die designs can now be implemented to take advantage of unique polymer character and to overcome the most critical processing difficulties. The models may also be used to eliminate certain polymers from consideration. Current efforts are to optimize the topocatheter material for maximally safe operation and to allow development of the topocatheter for arterial dilatation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10201-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Automated Cell Colony Scanner System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Dr. Seth Goldstein, Chief, Mechanical Engineering Section, BEIB, DRS
Dr. Michael Brownstein, Chief, Laboratory of Cell Biology, NIMH

COOPERATING UNITS *(if any)*

Laboratory of Cell Biology, NIMH

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.65	.5	.15

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A system will be developed for the purpose of identifying, for subsequent cloning, a minute fraction of cells possessing a specific antibody or other fluorescent tag. Major emphasis will be put on making the system as simple and inexpensive and readily available to investigators as possible. A variety of concepts and techniques have been identified and evaluated, and the most promising will be developed into a computer controlled instrument.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10202-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Optical Techniques for Dental Instrumentation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
G.M. Maxwell, Senior Staff Fellow, BEIB, DRS
R.L. Webber, Chief Diagnostic Systems Branch, CIB, NIDR

COOPERATING UNITS *(if any)*
CIB, NIDR

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.25	.25	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Two issues of importance in clinical dentistry are the assessment of a tooth's viability and the detection of caries in the regions where there is contact between adjacent teeth. Optical techniques are currently being explored as alternatives to present methods of measurement. Tooth viability is being examined by developing a system which can detect the presence of hemoglobin in the tooth by its absorption characteristics. The presence of caries between teeth is being assessed by measuring the fluorescence spectra which change with the development of tooth decay.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10203-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Clinical Assessment of Arterial Mechanical Properties

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
G.M. Maxwell, Senior Staff Fellow, BEIB, DRS
R. Chadwick, Biomedical Engineer, BEIB, DRS
D. Goldstein, Senior Investigator, IR, HE, NHLBI

COOPERATING UNITS *(if any)*
IR HE, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.25	.25	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this research is to develop an appropriate instrumentation system and associated data analysis techniques for evaluating the in-vivo mechanical properties of the brachial artery. Of particular interest is arterial distensibility, which can be evaluated in several ways. The most straightforward technique involves simultaneous measurement of arterial pressure and vessel diameter. An indirect and qualitative approach is also possible by analysis of the velocity waveform, a technique which can be performed non-invasively. Additionally, there are several theoretical formulations for arterial distensibility. Work on this project will be directed towards evaluating these various techniques to determine the limitations and advantages of each and to develop an instrumentation system suitable for routine clinical assessment of arterial mechanical properties.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10204-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cell Handling Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S.B. Leighton, Mechanical Engineer, BEIB, DRS
J.A. Berzofsky M.D., DCBD, NCI

COOPERATING UNITS *(if any)*

DCBD, NCI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

It is desireable to handle and process individual cells for monoclonal antibody work and other research endeavors. We are investigating a number of modalities for this, including flow cytometry, micromanipulators, dielectrophoresis, micropipettes, microtitre trays, and tissue culture techniques. We are considering sorting, storing, transporting and selectively inactivating cells. In addition, we are considering magnetic, gradient density, antigen-antibody, and solubility difference methods as possible candidates for separation techniques.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10205-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Constant Shear Field Apparatus for ESR Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S.B. Leighton, Mechanical Engineer, BEIB, DRS
H. Kon, Reserach Chemist, LCP, NIADDK

COOPERATING UNITS *(if any)*

LCP, NIADDK

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.1	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Electron Spin Resonance (ESR) is a valuable technique for studying membrane bound proteins. In particular, it can be used to study labeled proteins in red blood cell membranes. In order to know the orientations of the proteins with respect to the membranes, it is necessary to orient the membranes with respect to the ESR device. A fluid shear field serves the purpose of orientation, since the red blood cells are discoid and distensible. However, flow in capillary tubes, although functional and simple, provides a non-uniform shear field due to the Poiseuille velocity distribution. We are planning to use a moving thin polyester tape to create a uniform shear field and hence sharper resolution of orientation and a better signal to noise ratio.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10206-01 BEI

PERIOD COVERED
January 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Concentration Uniformity by Diastolic Phasing of Pulsed Intra-Arterial Infusions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
D.R. Shook, Biomedical Engineer, BEIB, DRS
J.L. Doppman, Chief, DRD, CC

COOPERATING UNITS *(if any)*
Diagnostic Radiology, CC (J.L. Doppman, M. Girton); Chemical Engineering Section, BEIB, DRS (R.J. Lutz, R.L. Dedrick)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.3	PROFESSIONAL: 0.3	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Inadequate infusate/blood mixing during intra-arterial chemotherapy at low catheter infusion rates (1 ml/min) produces highly nonuniform downstream drug concentrations. Inadequate treatment of the lesion and overexposure of normal tissues may result. Studies are underway to investigate the advantage of diastolically phased, high flow rate, pulsed intra-arterial infusions in effecting uniform downstream concentrations. Triggered by the ECG, a high velocity pulse during the interval of lowest blood velocity and retriggered on successive cardiac cycles, will yield average flow rates at the desired therapeutic value. Apparatus to produce that pulsed flow and methods of *in vivo* evaluation of downstream concentration uniformity are being developed. Highly realistic flow studies in an accurate model of the superior carotid artery and cerebral branches have demonstrated essentially complete concentration uniformity as determined by spectrophotometric comparison of infusate dye concentrations in all downstream branches. Upon optimization of the apparatus for animal and clinical use, and determination of appropriate clinical evaluation methods, pulsed intra-arterial infusions will be used in low flow rate clinical chemotherapeutic treatments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10207-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Clinical Engineering Program for Hospital Patient Care Areas

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
R. Corsey, Electronic Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
OD CC

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This program has evolved from the Electrical Safety Program for patient care areas. It is designed to provide preventative maintenance for patient care equipment, electrical safety testing for equipment both clinical and research in nature, and electrical safety for patient care areas. Auxiliary services provided include incident investigation for equipment failure and misadventures, and education of medical and support personnel regarding equipment hazards and guidance for utilization of electronic technology in patient care. In addition this program assures hospital compliance with patient care electrical standards of the Joint Commission on Accreditation of Hospitals and the Health Care Facilities section of the National Electric Code.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10208-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Hemodynamic Principles in the Control of Coronary Blood Flow

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
Thomas L. Talbot, MS, ACES, BEIB
Stephen E. Epstein, M.D. Cardiology, NHLBI
Richard O. Cannon, III, M.D. Cardiology, NHLBI

COOPERATING UNITS *(if any)*
Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 1.5	PROFESSIONAL: 1.5	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The effects of atherosclerotic epicardial stenosis on coronary vascular resistance can be understood in terms of basic fluid mechanical principles. Resistance is directly related to the trans-stenotic pressure drop and inversely related to flow. However, even with a fixed anatomic stenosis, resistance is not fixed; it increases as trans-stenotic flow increases. This exacerbates the pressure drop across the stenosis that develops as a result of flow; at high flows, large pressure drops can occur. This characteristic of flow through stenotic lesions can contribute to a "steal" physiology, between either epicardial or intramural coronary arteries. Studies have also shown the clinical importance and influence of dynamic alterations in coronary resistance, occurring either at the large or small vessel level. In addition, compressive forces exerted by the myocardium or by elevated intraventricular pressures can increase coronary vascular resistance, and therefore can interfere with myocardial perfusion. All these factors must be considered in order to understand the mechanisms leading to myocardial ischemia, and therefore to the clinical syndrome of angina pectoris.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10209-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Evaluation of Disposable Blood Pressure Transducers

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
E.C. Walker, Mechanical Engineer, ACES, BEIB
T.L. Talbot, Mechanical Engineer, ACES, BEIB
R.E. Clark M.D. Chief, Heart Surgery, NHLBI
D. Lawson M.D.

COOPERATING UNITS *(if any)*
NHLBI, Heart Surgery
CC, ICU
CC, Anesthesiology

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2	1.7	0.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A sample of each manufacturer of disposable blood pressure transducers was tested for compliance to AAMI's specifications for these devices. The data are currently being compiled for presentation to those responsible for placing these devices in use throughout the Clinical Center. The data does not represent an official endorsement of a particular device.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10210-01 BEI

PERIOD COVERED
May 4, 1984 to June 10, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Electronic Patient Monitoring

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
H.E. Cascio, Electronic Engineer, BEIB, DRS
R. Corsey, Electronic Engineer, BEIB, DRS
D. Cirelli, Administrator Officer, CC, OD
K. Musallam, Nurse, CCNURS

COOPERATING UNITS *(if any)*
CCOD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
EEES and ACE

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS: 0.4	PROFESSIONAL: 0.2	OTHER: 0.2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An electronic patient monitoring system that would alert the nursing staff when a patient (or patients) is leaving the nursing unit would be a welcome aid in the care of Alzheimer's disease patients. The system designis based on a wrist watch size radio transmitter, worn by the patient, with each transmitter having a different modulating frequency. A detector unit, placed at the two exit locations, would sense the presence of any patients in these exit areas. The detection of a patient's transmitter would activate an alarm at the nurses' station and would also generate a display giving the area and the name of the exiting patient. This system would be built for the 12 E Aging PCU but would also be of use for other units having similar needs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10211-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
IEEE-488 GPIB and Personal Computer Instrumentation Use Program Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.R. Clem, Sr., Electronic Engineer, EEES, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.2	0.05

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The increased availability and reduced cost of the small Personal Computer has created increased interest in automating data acquisition and process or experiment control in areas where such things were not feasible before due to cost or complexity. With these changes also came a significant increase in the use of the IEEE-488 GPIB by instrument makers. By combining the two, sophisticated instrumentation and data acquisition systems can be assembled quickly and inexpensively. The BEIB is continuing to develop the expertise to provide guidance and assistance to requirements where this approach provides the optimum solution. This capability is further assisted by the BEIB-SERP specifying the IEEE-488 interface on new equipment acquisitions whenever possible. The increase at the NIH in the numbers and use of the IBM PC has made this capability of great value to the NIH Intramural Research program.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10212-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Fluoroimmunoassay Apparatus

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W.S. Friauf	Ch., EEES	BEIB, DRS
R.L. Berger	Physicist	LTD NHLBI
G. Hemphill	Electronic Tech.	BEIB, DRS

COOPERATING UNITS *(if any)*

CDC, Atlanta

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.3	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

New rare earth chelate fluorescent probes with a decay time constant much longer than the background decay time-constant of typical organic materials offer the potential of a great improvement in sensitivity by appropriate timing of the response. However, to rival radioimmunoassay methods the required sensitivity improvement is so great that overload recovery of the fluorescence detector is a major problem. Extensive past work on this problem is largely inapplicable to the very low speed and level requirements of this situation. Consequently initial effort is being applied to determining the optimum fluorescence detection device and ancillary signal overload limiting circuitry. Problems related to the fluorescent probe at extremely low sample concentrations will be studied in collaboration with CDC, which is interested in this approach as another tool for AIDS research. Finally an evaluation of the details of excitation, optical filtering, and digital signal processing will be worked out and optimized.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10213-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Vitreous Fluorophotometry Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.M. Bungay	Chemical Engineer	BEIB,	DRS
R.F. Bonner	Biophysicist	BEIB,	DRS
M.S. Roy	Ophthalmologist	CB,	NEI
M.J. Podgor	Statistician	BE,	NEI

COOPERATING UNITS *(if any)*

Clinical Branch, NEI; Office of Biometry & Epidemiology, NEI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Vitreous fluorophotometry (VFP) is a clinical procedure for measuring the spatial distribution of fluorescence along the optical axis in a human subject's vitreous following administration of a fluorescent dye. In this project the clinical instrument is a Fluorotron Master manufactured by Coherent, Palo Alto, CA, and the dye is sodium fluorescein given by intravenous injection. The purpose of the project is to improve the protocols for conducting the measurements, processing the output from the instrument and analyzing the results from the population of normal volunteers and patients.

One disease to be considered is diabetes and the associated pathology diabetic retinopathy. The goals are to evaluate the procedure for use in (1) screening for early detection, and (2) monitoring for treatment efficacy. A pharmacokinetic mathematical model has been developed which describes the rate of appearance of fluorescein in the vitreous in terms of the blood-retinal barrier permeability (characterized by permeability coefficients of the retina-vitreous interface) and transport of fluorescein within the vitreous by diffusion (characterized by a diffusion coefficient). Plasma protein binding of fluorescein is also incorporated. Measurements have been made on 22 normal volunteers to evaluate the performance of the instrument, establish baseline parameter ranges, and critique existing protocols/analysis schemes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10214-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Photoradiation Therapy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D. Smith,	Physicist,	BEIB, DRS
R.F. Bonner	Physicist	BEIB, DRS
A. Russo		ROB, NCI
Z. Tochner		ROB, NCI

COOPERATING UNITS *(if any)*
Radiation Oncology Branch, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, Md 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An ascitic murine tumor, embryonal ovarian cell carcinoma, was used as a model of human ovarian carcinoma restricted to the peritoneum. The tumor was treated with a combination of hematoporphyrin derivative and intra peritoneal 514 nm light. Four HPD/laser treatments at 2 day intervals resulted in an 85% cure rate as determined by >100 day survival (untreated mice die between 20 and 23 days following the introduction of the tumor). Toxicity studies of the HPD/laser treatment are being carried out on dogs as a preliminary step for treatment of human patients. The possibility of using singlet oxygen fluorescence as a method of dosimetry is being evaluated.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10215-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Measurement of Trace-Level Metals and Complexes in Biological Milieux

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A.F. LeRoy, Ph.D., BEIB, DRS
M. Linnoila, M.D., Ph.D., CPB, NIMH
K. Flora, Ph.D., PRB, NCI
M.K. Wolpert, Ph.D., Drug Eval. Br., DCT, NCI
P. Galle, Prof. of Biophysics, Medical Faculty, Creteil, France
B. Hecquet, Ph.D.. Centre Oscar Lambret, Lille France
P. Parsons, Ph.D., BEIB, DRS

COOPERATING UNITS *(if any)*
CPB-NIMH, DCT-NCI, PRB-NCI, Biophysics Dept., Med. Faculty, Creteil, France: Centre Anti-cancereux "Oscar Lambret", Lille, France

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Analytical Methods

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.75	1.25	0.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Analytical methods have been developed for quantitation and characterization of metallic elements in biological samples. Analysis of vanadium in samples from human subjects under study has been conducted. Results obtained have shown very low values, in the range of nanograms-of-vanadium-per-gram of sample. Such results are obtained only with great difficulty because of the very small amount of sample available. Specific interest in platinum complex behavior of several different compounds used clinically has been studied. Chromatographic techniques are used to make separations of species in solutions. Atomic Absorption spectroscopy with electrothermal atomization(ETA-AAS) is used to quantitate total platinum or single isolated species. HPLC separation with electrochemical detection using a modified polarographic analyzer permits quantitation of the parent CDDP complex in aqueous solutions with a detection limit of about 50 ppb. Analytical methods developed have been used to make kinetic studies of behavior of platinum species from cisplatin in solution.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10216-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Enzyme Purification - Calmodulin

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
A.F. LeRoy Ph.D., BEIB/DRS
R. Berger, Ph.D., LTD, NHLBI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Analytical Methods

INSTITUTE AND LOCATION
National Institutes of Health, Behtesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.1	0.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Validity of studies characterizing and measuring properties of calmodulin depend on having quantifiable measures of purity of the enzyme preparation and the proportion of calcium it contains and requires the availability of extremely pure reagents, buffer, and solvents and contamination free labware.

Analytical methods have been developed for quantitaiton of picogram quantities of calcium in highly purified preparations of calmodulin and in the reagents and solvents needed to make the preparations. Preliminary analyses show that the needed reagents and solvents for making ultra-pure enzyme preparations can be freed to satisfactory levels from such ubiquitous contaminants as calcium using techniques developed in our laboratory.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10217-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Compact, Time-Domain Displays of Speech Signals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H.S. Eden, M.D., Ph.D., Deputy Chief, BEIB, DRS
M. Eden, Ph.D., Chief, BEIB, DRS
M.H. Goldstein, Ph.D., The Johns Hopkins University
J.M. Heinz, Ph.D., The Johns Hopkins University

COOPERATING UNITS *(if any)*
Department of Electrical Engineering and Instrumentation Branch

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Office of the Chief

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.5	.5	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this work was to develop a display of speech signals that provides useful, visually extractable information supplementary to that apparent in spectrograms. The approach was to develop and analyze pitch-synchronous displays of the acoustic pressure wave in which successive pitch intervals of voiced speech are time-aligned and closely spaced. Methods were developed for automated and semi-automated epoch extraction, based upon the nearest-neighbor algorithm and extrapolations from pitch-period contours. Theoretical studies relevant to such displays included the effects of the fundamental frequency of vocal fold oscillation on the time waveform, the effects of locally zeroing the spectral phase of time signals, and the mathematical relationship existing between spectrograms and pitch-synchronous time-domain displays. Through a known generalization of Shannon's sampling theorem, it was shown that the line spectrum of voiced speech is generally an undersampled version of the spectral envelope associated with a given vocal tract configuration; using a theorem by Linden and Abramson, conjectures were developed on ways that listeners might use the "jitter" normally found in speech to compensate for such undersampling and to aid constancy in perception of a vowel's identity as it is heard at different pitches.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10218-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Composition of Chromaffin Secretory Granules by Analytical Electron Microscopy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Visiting Scientist	BEIB, DRS
Others:		
R.L. Ornberg	Biophysicist	LCBG, NIADDK
C.E. Fiori	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*
Computer Systems Laboratory, Division of Computer Reserach and Technology, NIH (K.E. Gorlen)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The elemental composition of the secretory granules of bovine adrenal chromaffin cells has been determined by a combination of electron energy loss spectroscopy and energy dispersive x-ray spectroscopy. Ultrathin cryosections of rapidly frozen cultured cells were prepared and transferred at -170°C into the Hitachi H700H analytical electron microscope using a Gatan cryotransfer sample stage. Specimens were dehydrated in situ by warming up to -100°C and spectra were recorded at this temeprature to help minimize mass loss due to radiation damage. Energy loss spectra were recorded in an attempt to determine the nitrogen-to-phosphorus ratio and hence to estimate the relative amounts of nucleotides, proteins and catecholamines in the granules. Energy dispersive spectra recorded at known dose were used to determine concentrations of potassium, calcium, chlorine, sodium and phosphorus. The results could be compared with existing data from isolated granules.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10219-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Quantitative Elemental Mapping of Rapidly-frozen Neural Tissue

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R. D. Leapman	Visiting Scientist	BEIB
Others:		
S.B. Andrews	Special Expert	LN, NINCDS
T.S. Reese	Chief	LN, NINCDS
C.E. Fiori	Physical Scientist	BEIB, DRS
C.R. Swyt	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*

Computer Systems Laboratory, Division of Computer Research and Technology, NIH (K. Gorlen)

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Elemental Maps showing the distributions of calcium, potassium and sodium have been obtained from freeze-dried ultrathin cryosections of rapidly-frozen mouse cerebellar cortex. The molecular layer of the cerebellum was imaged by emission of characteristic x-rays with the use of an energy dispersive spectrometer on the BEIB analytical electron microscope. Data were obtained from resting or from repetitively stimulated tissue in order to investigate changes in ion distribution that occur on excitation. There was particular interest in determining the location of calcium concentrations that may be involved as intracellular stores required for transmission of nerve impulses. It was necessary to establish practical limits for calcium detection in an elemental map. Since the image is obtained serially, sensitivity depends on the number of pixels, ie. on the image resolution. In practice, concentrations of about 10-20 mmol/kg wet weight could be detected.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10220-01 BEI

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Elemental Imaging of Alzheimer's Disease Related Brain Tissue

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.E. Fiori, Physical Scientist, BEIB, DRS
David Nochlin, Senior Staff Fellow, LN, NIA
C.R. Swyt, Physical Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*

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☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Images of the distributions of calcium and aluminum in various brain tissues are being acquired by wavelength dispersive x-ray spectrometry in a Cameca MBX microprobe. The tissues are obtained by autopsy from patients exhibiting the clinical and pathological symptoms of Alzheimer's Disease and matched controls, and from rats fed an aluminum-rich diet and controls.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10221-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Elemental Imaging of Alveolar Macrophages

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
C.R. Swyt, Physical Scientist BEIB, DRS
C.E. Fiori, Physical Scientist, BEIB, DRS
R.D. Leapman, Visiting Scientist, BEIB, DRS
W. Rom, Senior Fellow, PB, NHLBI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Refractile particles are observed by light microscopy (LM) in alveolar lavaged macrophages from patients exhibiting clinical symptoms of asbestosis, silicosis and coal-miner's emphysema. However the elemental composition and location of these particles in the ultrastructure of the macrophages cannot be determined by LM. Elemental x-ray images obtained in the CAMECA MBX microprobe from large fields of whole air-dried macrophages have enabled investigators to correlate particle composition with disease. High resolution images of individual macrophages in ultrathin sections of epon embeded preparations obtained in the Hitachi H700H analytical electron microscope utilizing bright field (BF), energy dispersive x-ray (EDS) and electron energy loss (EELS) signals have revealed both elemental composition and ultrastructural location of the particles.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10222-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Elemental Distributions in Central Nervous System Tissues

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.R. Swyt	Physical Scientist	BEIB/DRS
R.M. Garruto	Senior Biologist	CNSS/NINCDS
C.E. Fiori	Physical Scientist	BEIB/DRS

COOPERATING UNITS *(if any)*
CNSS/NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

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Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.5	.5	–

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The occurance of neurofibrillary tangles and plaques is common to a number of central nervous system disorders including Guamanian amyotrophic lateral sclerosis (ALS), parkinsonism with dementia (PD), and Alzheimer's disease. These NFTs and plaques contain nonessential metals and elevated levels of biological elements. Fixed and frozen thick sections of hippocampus and frontal cortex of human brain from subjects exhibiting symptoms of these diseases have been examined in the CAMECA MBX microprobe. Wave length dispersive x-ray spectrometry (WDS) performed at selected areas has provided both spectra and digital images showing the distribution of elements of interest in the specimens.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10223-01 BEI

PERIOD COVERED

August 1, 1984 to August 1, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Individual Human Peripheral Mononuclear Cell Magnesium Quantitation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

G.R. Hook, Staff Fellow, Bioengineering and Instrumentation Branch, DRS
R.J. Elin M.D., Ph.D., Chief, Clinical Pathology Department, Clinical Center

COOPERATING UNITS *(if any)*

Clinical Pathology Department, Clinical Center

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Electron Beam Imaging and Microspectroscopy Group

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TOTAL MAN-YEARS: 1	PROFESSIONAL: 1	OTHER:

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☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Total body magnesium (Mg) is inversely correlated with heart disease, atherosclerosis and hypertension. Serum Mg is a poor indicator of total body Mg but peripheral blood mononuclear cell Mg may be a good indicator. Peripheral blood mononuclear cells are a heterogeneous population of lymphocytes and monocytes, with monocytes being twice the volume of lymphocytes. To evaluate mononuclear cell Mg, the mean cell Mg of the population, the individual cell Mg distribution within the population and the relationships between cell Mg and cell size must be determined. Whereas atomic absorption spectroscopy (AAS) methods have been developed to measure the mean mononuclear cell Mg, methods for measuring the Mg of individual mononuclear cells have not been described. We have developed a method for the quantification of Mg in individual whole mononuclear cells by electron probe X-ray microanalysis (EPMA). Whole blood is anticoagulated with heparin, washed with buffered saline glucose and ultracentrifuged in a discontinuous stractan density gradient. Isolated mononuclear cells are washed with isoosmotic, pH neutral ammonium nitrate, spray deposited on thin film supports, air dried and carbon coated for EPMA. The Mg concentration is determined by the peak-to-local continuum X-ray intensity ratio. Glass microsphere standards obtained form the National Bureau of Standards were used to calibrate the analysis. The mean cell Mg concentrations determined by AAS and EPMA were not significantly different. The coefficient of variation for replicate analysis of the standard by EPMA was 10%. The net variation in Mg concentration among individual cells was 20% and the distribution was symetrical. The Mg concentration was independent of cell size but the cell Mg content (fg/cell) increased with cell size.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10224-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Modified Fourier Transform Techniques

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
Michael Unser, Visiting Fellow, BEIB/DRS

COOPERATING UNITS *(if any)*

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☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Discrete Fourier Transform is widely used in signal processing for the computation of correlation or convolution equations. The aim of this project has been to study some alternatives that may be more suited for the processing of real signals. The definition of a class of transforms with pseudo-cyclic convolution properties has led to the discovery of a modified Fourier transform that allows efficient computation of aperiodic convolutions. In contrast to conventional Fourier transform techniques, this method does not require zero padding to suppress wraparound or aliasing errors. It requires less memory and less computation time than conventional complex algorithms.

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PROJECT NUMBER
Z01 RS 10225-01 BEI

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Processing of High Resolution Electron Micrographs

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
Michael Unser, Visiting Fellow, BEIB/DRS
Thierry Pun, Visiting Fellow, BEIB/DRS
Benes Trus, Research Chemist, CSL/DCRT
Alasdair C. Steven, Visiting Scientist, LPB/NIADDK

COOPERATING UNITS *(if any)*

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☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

High resolution micrographs are often of poor quality, due to various distortions and especially to a very low signal-to-noise ratio. Visual quality can be improved significantly by appropriately combining several observations of similar subjects. The aim of this project is to develop signal processing techniques to facilitate structure determination from such electron micrographs. Methods for translational and rotational alignment of different views of the same subject have been developed and implemented. Principal components and correspondence analysis have been used to seek important characteristics of the data. A procedure for automated statistical rejection of outlying samples has been proposed. These methods have been applied successfully to the structure determination of Herpes and T7 viruses by combining as many as 50 different observations of the same object.

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